Intraoperative Transcranial Motor-Evoked Potential Monitoring of the Facial Nerve during Cerebellopontine Angle Tumor Resection

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Abstract

Objective To determine whether transcranial motor-evoked potential (TCMEP) monitoring of the facial nerve (FN) during cerebellopontine angle (CPA) tumor resection can predict both immediate and long-term postoperative FN function.

Design Retrospective review.

Setting Tertiary referral center.

Main Outcome Measures DeltaTCMEP (final-initial) and immediate and long-term facial nerve function using House Brackmann (HB) rating scale.

Results Intraoperative TCMEP data and immediate and follow-up FN outcome are reported for 52 patients undergoing CPA tumor resection. Patients with unsatisfactory facial outcome (HB > 2) at follow-up had an average deltaTCMEP of 57 V, whereas those with HB I or II had a mean deltaTCMEP of 0.04 V ($t = -2.6$, $p < 0.05$.) Intraoperative deltaTCMEP did not differ significantly between groups with satisfactory (HB I, II) and unsatisfactory (HB > 2) facial function in the immediate postoperative period.

Conclusion Intraoperative TCMEP of the facial nerve can be a valuable adjunct to conventional facial nerve electromyography during resection of tumors at the CPA. Intraoperative deltaTCMEP >57 V may be worrisome for long-term recovery of satisfactory facial nerve function.

Keywords

- facial nerve
- cerebellopontine angle
- intraoperative electrophysiologic monitoring
- transcranial motor-evoked potential

Introduction

Preservation of facial nerve (FN) function is a well-recognized goal of tumor excision at the cerebellopontine angle (CPA). Especially in cases of vestibular schwannoma excision, postoperative facial paresis and paralysis may occur despite efforts to avoid injury and maintain anatomic integrity of the nerve during dissection. Introduced by Delgado in 1979, intraoperative monitoring with continuous electromyogra-

phy (EMG) is now routine and has been shown to improve FN functional outcome.^{1–5} Continuous EMG identifies neurotonic discharges generated by mechanical or metabolic stimuli and can alert the surgeon to possible facial nerve injury from surgical manipulation. One particular pattern of discharge, the “A train,” is prolonged, surgery-related activity that has been shown to correlate highly with postoperative facial nerve dysfunction.^{6–8} Until recently, however, real-time analysis of these trains was not possible and therefore

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of limited utility for intraoperative decision-making. Direct electrical stimulation can be used intermittently to assist with identification and mapping of the facial nerve location during tumor resection. Amplitude of the compound muscle action potentials (CMAPs) evoked by direct stimulation, as well as the threshold stimulation intensity (mA), can provide a functional assessment of the nerve and have been shown to correlate with postoperative facial nerve outcomes.^{9–15} However, triggered CMAP generation implies functional integrity only between the site of direct stimulation and the recording electrodes and, therefore, requires FN identification at the brainstem. This method can be of limited utility when the nerve course and/or its emergence from the brainstem is inaccessible or obscured by tumor bulk at the CPA.

In contrast, motor-evoked potential monitoring of the FN using transcranial stimulation of the motor cortex (TCMEP) yields information regarding the full facial nerve pathway without requiring direct nerve stimulation. Reliably employed in spine and intracranial surgery, transcranial generation of extremity muscle motor-evoked potential (MEP) allows intraoperative feedback regarding the functional integrity of the motor cortex, corticospinal tract, α motor neurons, peripheral nerve, and neuromuscular junction.^{16–19} Recently, transcranial stimulation techniques have been applied to intraoperative facial nerve monitoring with favorable results.^{20–26} Studies indicate that TCMEP of the facial nerve is feasible and may predict immediate postoperative outcome. Long-term functional data and the relationship between TCMEP and facial nerve function beyond the immediate postoperative period is lacking.

The goal of the present study was to determine if intraoperative TCMEPs can predict immediate and long-term postoperative facial nerve function in patients undergoing CPA tumor resection.

Methods

Patients

Intraoperative TCMEPs were recorded from 52 patients undergoing surgery for tumors at the cerebellopontine angle from April 2009 to March 2010 at New York University Langone Medical Center. Patients ranged in age from 21 to 73 years old (mean 49.5 years), 56% were female, and 29 tumors were on the left (—Table 1). Tumor pathology included vestibular schwannomas, meningiomas, epidermoid, and neurofibromatosis type 2 (NF2). Excision was accomplished using a variety of approaches, specifically translabyrinthine, retrosigmoid, and middle cranial fossa. Two patients had received prior Gamma Knife radiosurgery with subsequent tumor growth, whereas one patient had prior microsurgical excision at another institution. All patients underwent full audiometric testing and magnetic resonance imaging (MRI) with gadolinium preoperatively. The majority of patients reported preoperative vestibular dysfunction ($n = 34$), described as imbalance, disequilibrium, and/or vertigo and tinnitus ($n = 34$.) Tumor size was measured on MRI in three orthogonal planes (anterior-posterior, transverse, and craniocaudal) and categorized into three groups based estimated

Table 1 Patient Characteristics, $N = 52$

	N (%)	Mean (Range)
Female	29 (56%)	
Left side	29 (56%)	
Age		49.5 (21–73)
Diagnosis		
Vestibular schwannoma	43 (83%)	
Meningioma	4 (8%)	
NF2	4 (8%)	
Epidermoid	1 (2%)	
Approach		
TL	18 (33%)	
RS	29 (56%)	
MCF	5 (9%)	
Prior Gamma Knife Radiosurgery	2 (4%)	
Recurrent tumor ^a	1 (2%)	
Tumor size ^b		
IC	5 (9%)	
<1.5 cm	19 (36%)	
1.5–3 cm	24 (46%)	
>3 cm	4 (8%)	
Tumor removal		
Total	42 (80%)	
Near- or Subtotal	10 (20%)	
Length of follow-up (months)		10 (1–26)

^aThis patient had prior microsurgical excision of this tumor.

^bSize categorization based on intracanalicular location and estimates of tumor diameter (anterior-posterior $\times$ transverse $\times$ craniocaudal) $\text{cm}^{1/3}$ HB, House-Brackmann facial nerve grading scale; IC, intracanalicular; MCF, middle cranial fossa; NF2, neurofibromatosis type 2; RS, retrosigmoid; TL, translabyrinthine.

tumor diameter ($\text{cm}^{1/3}$): <1.5 cm ($n = 19$), 1.5 to 3 cm ($n = 24$), and >3 cm ($n = 4$).²⁷ Tumors that were confined to the internal auditory canal and did not extend into the cerebellopontine angle cistern were categorized as intracanalicular ($n = 5$.) Brainstem indentation and/or compression of the fourth ventricle on MRI was found in 21 patients.

Total tumor removal was accomplished in 42 patients (80%). The remaining patients ($n = 10$) had near- or sub-total tumor removal. Anatomic integrity of the facial nerve was preserved in all cases and no patient required intraoperative facial nerve grafting to repair a severed or truncated nerve. Facial nerve function was evaluated pre-operatively, immediately postoperatively, and at follow-up using the House-Brackmann scale.²⁸ Immediate postoperative values were obtained within 48 hours of surgery. Follow-up data was available from 1 to 26 months after surgery (mean 10 months).

Anesthesia and Intraoperative Monitoring

In all cases, anesthesia was delivered by a neuroanesthesiology team experienced with CPA surgery and the requirements of neural monitoring. Induction was accomplished with fentanyl, propofol, and a single dose of a short-acting agent for neuromuscular blockade. Following intubation, general anesthesia was maintained with a continuous infusion of propofol (100 to 150 $\mu\text{g/kg/min}$) supplemented with remifentanyl. Halogenated anesthetics were not used and bolus injections were generally avoided.

TCMEP monitoring of the facial nerve was performed using corkscrew scalp electrodes (Nicolet Biomedical Inc., Fitchburg, WI, USA) placed at positions C3, C4, and Cz (International 10–20 EEG electrode system, ► **Fig. 1**). Potentials were recorded from paired subdermal needle electrodes placed in the orbicularis oris. All intraoperative monitoring was performed by a single, experienced neuroelectrophysiologist. TCMEP recording began prior to skin incision and continued until wound closure, occurring approximately every 10 to 20 minutes during tumor excision or upon request of the operating surgeons. The Endeavor monitoring system (Nicolet Biomedical) was used for voltage stimulation, recording, and data capture. Multipulse stimulation was employed with an interstimulus interval of 4 milliseconds, duration of 0.2 to 0.5 milliseconds, rate of 1.0 Hz, train rate of 250–450 Hz, train count of 3 and stimulation of 50–350V. To exclude the potential issue of current spread and peripheral facial nerve activation, the response with a long-duration polyphasic waveform and long-onset latency of more than 12 milliseconds was defined as the FN MEP.

Additional intraoperative monitoring consisted of somatosensory evoked potentials (SSEP), motor-evoked potentials of the extremities, continuous EMG of the facial nerve and, when appropriate, auditory brainstem response (ABR) testing. In select cases, continuous EMG of the lower cranial nerves, such as the vagus nerve, were performed. Direct electrical stimulation of the facial nerve using a handheld

stimulating probe was performed routinely and intermittently during surgery at the discretion of the operating surgeon.

Statistical Analysis

Mean and deltaTCMEP (final-initial) values were calculated for each patient. Patients were divided into two groups based on facial nerve function at discharge and at follow-up evaluation: HB grade I or II (satisfactory) and greater than HB grade II (unsatisfactory). Independent samples tests were used to analyze the relationship between intraoperative deltaTCMEP and postoperative facial nerve function. An unequal variance *t*-test was used to compare patients with satisfactory and unsatisfactory FN outcome at immediate and follow-up evaluation in terms of deltaTCMEP and to compare patients defined in terms of selected binary factors (such as preoperative tinnitus, vestibular symptoms). Logistic regression models were applied to assess the ability of deltaTCMEP and additional variables (including diagnosis, route, tumor size) to predict postoperative facial nerve function either immediately or at follow-up. All reported *p* values are two-sided, and statistical significance was defined as $p < 0.05$. SAS 9.0 (SAS Institute, Cary, NC, USA) was used for all computations.

Results

Preoperatively, nearly all patients had normal preoperative facial function, with three patients demonstrating mild dysfunction, HB grade II (► **Table 2**). Of these three patients, two improved to normal function, HB grade I, at follow-up. The remaining patient demonstrated severe dysfunction, HB grade V, immediately postoperatively and returned to a HB grade II at follow-up.

Immediately postoperatively, 68% of the study population demonstrated normal (HB grade I, $n = 32$) or mild facial dysfunction (HB grade II, $n = 4$), and the remainder exhibited moderate to severe paresis (HB grade III–V, $n = 11$) or total paralysis (HB grade VI, $n = 5$). After hospital discharge, follow-up data was taken from the last follow-up date, ranging from 1 to 26 months following surgery (mean 10 months). At latest follow-up, 90% of patients had normal ($n = 38$) or mild dysfunction (HB grade II, $n = 9$). Four of the remaining patients had moderate-moderately severe function (HB grade III–V) and one patient continued to exhibit complete flaccid paralysis (HB grade VI) (► **Table 3**). The latter patient underwent delayed facial reanimation surgery with hypoglossal-facial nerve anastomosis ~10 months following vestibular schwannomas excision and remained with total paralysis at last follow-up, 4 months after reanimation. Five patients demonstrated complete paralysis at immediate follow-up. Of these, two patients improved to HB grade II, two improved to HB grade III, and only one (previously mentioned) required a facial reanimation procedure.

DeltaTCMEP (final-initial) values ranged from 0 to 57 V. Average deltaTCMEP was 3.9 V (standard deviation [SD] 47.1) in patients with satisfactory function (HB grade I or II) immediately postoperatively ($n = 36$) and 10.9 V (SD 78.5) in patients with unsatisfactory ($n = 16$) immediate function.

Figure 1 Diagram of the International 10–20 EEG electrode system highlighting stimulating electrodes C3, C4, and Cz used in transcranial motor-evoked potential monitoring of the facial nerve.

Table 2 Preoperative, Immediate and Follow-up Facial Nerve Outcomes ($N = 52$)

HB Grade	N (%)
Preoperative	
I	49 (94%)
II ^a	3 (6%)
Immediate postoperative	
Satisfactory	36 (68%)
I	32
II	4
Unsatisfactory	16 (32%)
III	5
IV	1
V	5
VI	5
Follow-up ^b	
Satisfactory	47 (90%)
I	38
II	9
Unsatisfactory	5 (10%)
III	3
IV	1
V	0
VI ^c	1

^aTwo of the three patients with preoperative HB grade II improved to normal function, HB grade I, at follow-up. The remaining patient demonstrated severe dysfunction, HB grade V, immediately postoperatively and returned to a HB grade II at follow-up.

^bFollow-up occurred between 1–26 months postoperatively (mean 10 months).

^cThis patient underwent delayed XII-VII anastomosis ~9 months after initial surgical excision. Follow-up data from this patient is obtained at 14 months after vestibular schwannoma excision (which is 4 months after facial nerve reanimation procedure.)

HB, House-Brackmann facial nerve grading scale.

Differences in mean deltaTCMEP between groups with satisfactory and unsatisfactory FN function in the immediate postoperative period were nonsignificant ($t = -0.36$, $p > 0.7$) (► **Fig. 2**).

For patients with satisfactory FN function ($n = 47$) at follow-up, average deltaTCMEP values approximated zero (0.04 V), meaning there was very little change in their MEP during surgery. In contrast, patients with unsatisfactory FN function at follow-up ($n = 5$) demonstrated an average deltaTCMEP of 57 V. Independent samples test showed the difference between intraoperative deltaTCMEP in patients with satisfactory and unsatisfactory FN function at follow-up was significant ($t = -2.6$, $p < 0.05$). (► **Fig. 3**) There were no differences between groups with satisfactory outcome and those with unsatisfactory FN outcomes in gender, age, side of tumor, pathology, approach, estimated tumor size, presence

of tinnitus or symptoms of vestibular dysfunction either immediately postoperatively or at follow-up. Using these variables and deltaTCMEP, logistic regression analysis did not find any model that effectively predicted unsuccessful outcome (HB > II) at follow-up.

Throughout each procedure, the operating surgeons maintained ongoing communication with the neuroelectrophysiologist regarding TCMEP monitoring of the facial nerve, especially during tumor dissection. Decreasing amplitudes and increasing voltage requirements were interpreted as potential indicators of functional damage to the facial nerve and were conveyed in real-time to the operating surgeon. The location of the facial nerve was reassessed, often using direct electrical stimulation. Occasionally, the stimulating probe revealed previously unidentified FN fibers in the field of dissection. Frequently, however, especially in the early stages of tumor resection of large tumors, direct electrical stimulation was uninformative, as the nerve was inaccessible and/or obscured by the tumor. Based on TCMEP monitoring suggesting possible functional compromise of the FN, the operating surgeon often modified the operative strategy, perhaps by changing the angle or location of tumor dissection or by changing the dissecting instrument. Decisions to halt tumor dissection or to perform sub- or near-total resections were never based on neurophysiologic monitoring (specifically the TCMEP) alone. A multitude of factors, including age, tumor size, preoperative function, blood loss and hemodynamic stability, facial EMG, and TCMEP monitoring guided intraoperative surgical strategy and decision making.

Discussion

Consistent with prior research, the present study suggests that transcranial stimulation of the facial nerve is a feasible and useful method of monitoring facial nerve function during surgery of the CPA. Although optimal stimulation parameters for TCMEP of the FN remain unknown, current data support previously published techniques using multipulse stimulation of 3 to 5 trains, duration 0.2 to 0.5 milliseconds, and interstimulus interval of 4 milliseconds.^{20–22,24} These parameters successfully minimized peripheral FN activation yet were able to overcome anesthesia-induced suppression of MEP. In addition to stimulation parameters, many factors are known to affect TCMEP monitoring, including anesthesia, use of muscle relaxants, number and type of recording electrodes, and individual patient variation.^{17,19,29} Close communication with an experienced neuroanesthesiology team accustomed to delivery of TCMEP-compatible anesthesia can be crucial for successful intraoperative neural monitoring.

Despite anatomic integrity of the FN during tumor dissection, unsatisfactory postoperative paresis and complete paralysis were encountered in 16 patients (32%) immediately after surgery. Eleven of these patients recovered facial function, including four of the five patients with complete paralysis, and many achieved HB grade I or II at follow-up evaluation. Etiology of immediate paresis/paralysis is incompletely understood, but may include a conduction block, neuropraxia or axonotmesis caused by intraoperative

Table 3 Patients with Facial Nerve Function Greater than HB II at Discharge or Follow-up

Sex/Age	Diagnosis	Approach	TCMEP				Tumor Size ^a	Removal	FN Function (HB Grade)			F/U (m)
			Min	Max	Mean	Delta			Pre-op	Immediate	F/U	
F/48	VS NF2	RS	108	160	129	-32	1.5-3	Total	1	3	1	14
M/18	VS	TL	116	156	134	40	1.5-3	Total	1	3	1	1
M/37	VS	RS	168	180	173	12	1.5-3	Total	1	3	1	12
M/50	Meningioma	RS	184	216	187	8	>3	Subtotal	1	4	1	4
F/63	VS	RS	140	144	143	0	<1.5	Total	1	3	2	5
F/49	VS	MCF	144	192	166	-48	IC	Total	1	5	2	12
F/59	VS	TL	76	312	242	-236	IC	Total	2	5	2	24
F/50	VS	TL	80	80	80	0	1.5-3	Near-total	1	5	2	24
F/47	VS	TL	164	204	166	-20	1.5-3	Near-total	1	5	2	20
F/44	VS	MCF	192	252	206	60	<1.5	Total	1	6	2	10
M/50	VS	RS	152	168	160	4	1.5-3	Total	1	5	2	6
F/66	VS	TL	152	276	220	124	1.5-3	Total	1	6	2	13
F/21	VS NF2	TL	140	172	164	-12	1.5-3	Total	1	3	2.5	22
M/33	VS (recurrent) ^b	TL	208	240	225	-12	<1.5	Total	1	6	3	6
M/54	VS	TL	236	256	249	8	>3 cm	Total	1	2	3	4
F/66	VS	RS	180	264	200	84	1.5-3	Total	1	6	3	9
M/62	VS	TL	140	200	166	60	>3 cm	Subtotal	1	6	6	14

^aSize categorization based on intracranial location and estimates of tumor diameter (anterior-posterior x transverse x craniocaudal) cm^{1/3}^bThis patient had prior microsurgical excision of this tumor.

F, female; FN, facial nerve; F/U, follow-up; HB, House-Brackmann facial nerve grading scale; m, months; M, male; MCF, middle cranial fossa; NF2, neurofibromatosis type 2; pre-op, preoperative; RS, retrosigmoid; TCMEP, transcranial motor-evoked potentials; TL, translabyrinthine; VS, vestibular schwannoma.

Figure 2 Box plot of mean delta transcranial motor-evoked potential (TCMEP) for patients with satisfactory (HB I, II; $n = 36$) or unsatisfactory (HB > II; $n = 16$) immediately postoperatively. Differences between the means were found to be nonsignificant ($p > 0.7$). Box range denotes the 25th and 27th percentile, and whiskers extend to the limit of the contiguous data points. The black band represents the 50th percentile (median).

mechanical/iatrogenic manipulation, edema, vasoconstriction/spasm of neuronal blood supply, herpes virus reactivation, or some combination of these. A temporary conduction block may recover rapidly, over a period of days, whereas neuropraxia or axonometesis may require months to improve and may not reach pre-operative function.¹⁵ This study suggests that intraoperative TCMEP data may be helpful in distinguishing patients in whom initial paresis/paralysis may ultimately improve to satisfactory facial function in the long-term. Patients with HB grade > II demonstrated changes in intraoperative TCMEP up to 57 V, whereas those with long-term satisfactory function had little to no change (0.04 V). Facial nerve dysfunction leads to significant morbidity, including difficulties in communication, oral intake, and ocular complications, and has significant cosmetic and social implications. Improved identification of patients at risk for unsatisfactory outcomes may direct early intervention and rehabilitative procedures to improve quality of life and prevent ocular complications.

Statistical analysis did not reveal a relationship between TCMEP, HB grade, and a variety of other factors, including age, tumor size, diagnosis, preoperative symptoms, or approach. It is possible that the small sample size prevented detection of

Figure 3 Box plot of mean delta transcranial motor-evoked potential (TCMEP) for patients with satisfactory (HB I, II; $n = 47$) or unsatisfactory (HB > II; $n = 5$) at follow-up. Differences between the means were found to be significant ($p < 0.05$). Box range denotes the 25th and 27th percentile, and whiskers extend to the limit of the contiguous data points. The black band represents the 50th percentile (median).

these correlations. It is also possible that FN outcome is significantly affected by variables that were not assessed, such as extent of tumor adhesion to the facial nerve sheath and course of the facial nerve. Bernat et al (2010) and others have demonstrated the predictive value of these surgical observations in postoperative facial nerve dysfunction.^{15,30-33}

Intraoperatively, TCMEP monitoring conveyed information about FN functional integrity that could not be obtained with either continuous EMG or direct electrical stimulation. Direct neural stimulation is an effective tool for distinguishing the facial nerve from adjacent structures and electrically mapping its location relative to the tumor; however, it is inherently intermittent, requiring the surgeon to discontinue dissection and introduce a stimulating probe to gain information. Additionally, in cases where the facial nerve has been significantly thinned and/or stretched by a large tumor, localized direct stimulation may not contact enough nerve fibers to allow action potential generation, thereby yielding inconsistent information about the location and integrity of the facial nerve. In contrast, transcranial stimulation of the motor cortex provides information on neural integrity even in cases where the nerve has been significantly thinned by a large tumor.

Although direct stimulation thresholds have shown prognostic value in predicting facial nerve outcome, the discontinuous nature of this technique may miss injurious manipulation and identify neural injury only after it occurs. Multiple techniques for continuous monitoring have been reported, the most common of which is continuous EMG with audio (loudspeaker). Experienced surgeons may recognize which acoustic signals correspond to worrisome neurotonic discharges, such as the "A trains" associated with postoperative nerve dysfunction, but objective guidelines and an ability

to quantify these trains are not available in most centers.⁷ Prell et al (2010) recently designed and implemented software for real-time analysis of neurotonic outbursts and demonstrated a significant correlation between quantitative "train time" and extent of postoperative facial deficit.⁸

In addition to small sample size, this study was limited by variability in the number and timing of TCMEP measurements per case, lack of a control side recording, variations in depth of anesthesia, and the subjective bias of facial nerve functional assessment (HB grade). Additionally, prior studies have utilized two recording sites, orbicularis oculi and oris, whereas the current study recorded only from the former. Future research is necessary to directly correlate TCMEP monitoring with techniques of continuous EMG and direct electrical stimulation. Ideal intraoperative FN monitoring technique would not only yield rapid diagnosis of iatrogenic injury, but it would provide real-time, continuous feedback to guide surgical strategy and prevent nerve dysfunction. TCMEP can be reliably and effectively used in combination with other methods of intraoperative FN monitoring to maximize long-term functional outcome.

Conclusion

Intraoperative transcranial MEP of the facial nerve can be a valuable adjunct to conventional facial nerve EMG during resection of tumors at the CPA. It may be especially useful when the facial nerve course is obscured by tumor bulk or inaccessible to direct electric stimulation. Intraoperative deltaTCMEP >57 V may be worrisome for long-term recovery of satisfactory facial nerve function. Further analysis of and experience with techniques of TCMEP for intraoperative FN monitoring are warranted.

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